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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/553,633	11/07/2006	Songtao Shi	4239-81540-05	4649

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EXAMINER	
FALK, ANNE MARIE	
ART UNIT	**PAPER NUMBER**
1632	

NOTIFICATION DATE	DELIVERY MODE
08/23/2010	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/553,633	SHI ET AL.	
	Examiner	Art Unit	
	Anne-Marie Falk, Ph.D.	1632	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2010*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *59-65,67,68,71-78,80-86,88-90 and 92-109* is/are pending in the application.

4a) Of the above claim(s) *67,68,71-78,80-86,88-90 and 92-102* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *59-65,103-107 and 109* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *19 October 2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

The amendment filed April 1, 2010 (hereinafter referred to as "the response") has been entered. Claims 59-65, 67, 78, 86, 89, 90, 103-108 have been amended and Claim 109 has been newly added.

Accordingly, Claims 59-65, 67, 68, 71-78, 80-86, 88-90, and 92-109 are pending in the instant application.

The elected invention is drawn to a dental pulp multipotent stem cell.

Claims 67, 68, 71-78, 80-86, 88-90, 92-102, and 108 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected invention, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on December 9, 2009.

Accordingly, Claims 59-65, 103-107, and 109 are examined herein.

The rejection of Claims 59-65 and 103-107 under 35 U.S.C. 102(a), as being anticipated by Gronthos et al. (August 2002, J. of Dental Research 81(8): 531-535), is **withdrawn** in view of the amendments to the claims. The reference does not disclose a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings. However, as noted in the new matter rejection hereinbelow, the instant specification also does not disclose a CD146-positive cell that can proliferate to over 140 population doublings.

The rejection of Claims 59-65 and 103-107, under 35 U.S.C. 102(b) as being anticipated by Gronthos et al. (2000, PNAS 97(25): 13625-13630), is **withdrawn** in view of the amendments to the claims. The reference does not disclose a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings. However, as noted in the new matter rejection hereinbelow, the instant specification also does not disclose a CD146-positive cell that can proliferate to over 140 population doublings.

The rejection of Claims 59-65 and 103-107 under 35 U.S.C. 102(b), as being anticipated by WO 02/07679 (Shi et al., January 2002), is **withdrawn** in view of the amendments to the claims. The reference does not disclose a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings. However, as noted in the new matter rejection hereinbelow, the instant specification also does not disclose a CD146-positive cell that can proliferate to over 140 population doublings.

The rejection of Claims 59-65 and 103-107 under 35 U.S.C. 102(b) as being anticipated by Shi et al. (2001, Bone 29(6): 532-539), as evidenced by Gronthos et al. (2000, PNAS 97(25): 13625-13630) and Gronthos et al. (August 2002, J. of Dental Research 81(8): 531-535), is **withdrawn** in view of the amendments to the claims. The reference does not disclose a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings. However, as noted in the new matter rejection hereinbelow, the instant specification also does not disclose a CD146-positive cell that can proliferate to over 140 population doublings.

The rejection of Claim 65 under 35 USC § 103(a), as being obvious over Gronthos et al. (2000, PNAS 97(25): 13625-13630) and Nakashima et al. (June 2002, Gene Therapy 9(12): 814-818), is **withdrawn** in view of the amendments to the claims. The reference does not disclose a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings. However, as noted in the new matter rejection hereinbelow, the instant specification also does not disclose a CD146-positive cell that can proliferate to over 140 population doublings.

Claim Objections

Claim 103 is objected to under 37 CFR 1.75(c), as being of improper dependent form for failing to further limit the subject matter of a previous claim. Applicant is required to cancel the claim(s), or amend the claim(s) to place the claim(s) in proper dependent form, or rewrite the claim(s) in independent

form. Claim 103 recites the limitation "wherein the stem cell has a higher proliferation rate than adult dental pulp cells and bone marrow stem cells." Claim 59, however, has been amended to recite the limitation "wherein the isolated human postnatal dental pulp multipotent stem cell can proliferate to over 140 population doublings" which already **is** a higher proliferation rate than adult dental pulp cells and bone marrow stem cells. Thus, Claim 59 is already limited to a stem cell having a higher proliferation rate than adult dental pulp cells and bone marrow stem cells. At page7, lines 14-15, the specification states that "SHED were able to proliferate to over 140 population doublings, which was significantly higher…than BMSCs and DPSCs." Therefore, the limitation of Claim 103 is now not further limiting.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

New Matter

Claims 59-65, 103-107, and 109 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The amended claims and newly added claim include new matter.

MPEP 2163.03(I) provides that an amendment to the claims or the addition of a new claim must be supported by the description of the invention in the application as filed. *In re Wright*, 866 F.2d 422, 9 USPQ2d 1649 (Fed. Cir. 1989). Applicants should specifically point out the support for any amendments made to the claims. MPEP 2163 states that new or amended claims which introduce elements or limitations which are not supported by the as-filed disclosure violate the written description requirement.

See, e.g., *In re Lukach*, 442 F.2d 967, 169 USPQ 795 (CCPA 1971) and *In re Smith*, 458 F.2d 1389, 1395, 173 USPQ 679, 683 (CCPA 1972). MPEP 714.02 notes that Applicant should also specifically point out the support for any amendments made to the disclosure. See also MPEP 2163.06(I), which notes that Applicants should specifically point out the support for any amendments made to the disclosure.

The claims have been amended to add the limitation "wherein the isolated human postnatal dental pulp multipotent stem cell can proliferate to over 140 population doublings." Accordingly, Claim 59 is directed to a CD146-positive cell that can proliferate to over 140 population doublings. However, the specification does not describe a CD146-positive cell that can proliferate to over 140 population doublings. On the contrary, the specification only describes a mixed population of cells (SHED) that can proliferate to over 140 population doublings.

As support for the amendment, Applicants point to the specification at page 7, lines 10-15 and Figure 5. However, the cited section clearly describes a mixed population of cells, designated as "SHED." The assessment of proliferation in terms of population doublings was carried out using this mixed population of cells (SHED). Notably, the specification does not provide an assessment of the proliferation of any particular cell type present within the mixed population. Thus, the rate of proliferation of the multipotent stem cell that is identified as residing within this mixed population of cells is unknown. Accordingly, the specification fails to describe a multipotent stem cell that can proliferate to over 140 population doublings. Instead, the specificationd describes a mixed population of cells (SHED) which can proliferate to over 140 population doublings. The proliferative capacity of any cell type within the mixed population is unknown. Thus, there is no evidence that a CD146-positive cell can proliferate to over 140 population doublings.

As amended, Claim 59 is directed to a CD146-positive multipotent stem cell that can proliferate to over 140 population doublings and can differentiate into a neural cell, an adipocyte, or an odontoblast.

However, there is no description of a CD146-positive cell that can proliferate to over 140 population doublings. While the specification does disclose that SHED were able to proliferate to over 140 population doublings (page 7, line 14), the specification makes it clear that SHED is a mixed population of cells (pages 27-28). See for example, the specification at page 8, lines 10-17, which discloses that only 25% of SHED clones were capable of generating dentin *in vivo*. At page 7, lines 17-21, the specification discloses that SHED expressed STRO-1 and CD146 and that FACS analysis of *ex vivo* expanded SHED showed that SHED contained approximately 9% STRO-1-positive cells. The specification is silent as to the percentage of SHED expressing CD146. However, there is no disclosure of CD146-positive cells that have the potential to undergo 140 population doublings. Only the mixed population of SHED is described as having the ability to proliferate to over 140 population doublings.

Likewise, with regard to Claim 61, the specification does not describe a STRO-1-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an ALP-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a matrix extracellular phosphoglycoprotein-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an bFGF-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an endostatin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 62, the specification does not describe a CBFA1-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an MEPE-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an BSP-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an DSPP-positive cell that can proliferate to over 140 population doublings. Nor does the specification

describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 63, the specification does not describe a osterix-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an osteocalcin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Likewise, with regard to Claim 64, the specification does not describe a nestin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an βIII tubulin-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a glutamic acid decarboxylase-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe an neuronal nuclei-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a glial fibrillary acidic protein-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a neurofilament M-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a 2'3'-cyclic nucleotide-3'-phosphodiesterase-positive cell that can proliferate to over 140 population doublings. Nor does the specification describe a cell that expresses a combination of these proteins and that can also proliferate to over 140 population doublings.

Given the many dependent claims to isolated human postnatal deciduous dental pulp stem cells, Claim 59 appears to cover a wide variety of stem cells expressing distinct sets of markers. Accordingly, Claim 59 is further rejected insofar as it encompasses the various cell types recited in Claims 61-65 because the specification fails to describe all the cell types encompassed by Claim 59. The dependent claims appear to be directed to various subsets of stem cells that fall within the broad independent claim

(i.e., Claim 59), but there is no description of distinct multipotent stem cells that are CD146-positive and that can proliferate to over 140 population doublings.

Newly added Claim 109 is directed to an *ex vivo* expanded population of the stem cell of Claim 59. Since the specification fails to describe the stem cell of Claim 59, for the reasons discussed above, the specification likewise fails to describe the ex vivo expanded population of Claim 109.

Since the as-filed specification does not describe the subject matter of Claim 59 and the various cell types recited in the dependent claims, claims directed to subject matter not disclosed in the originally filed specification cannot be introduced after the application filing date. Such a claim raises an issue of new matter. Given the newly added limitation, the specification would have to provide support for the multipotent stem cell of Claim 59, in its broadest sense, and multiple distinct cell types as set forth in the dependent claims. However, the specification does not provide broad support, nor does it provide narrower support for cells expressing the various proteins recited in the claims and also having the ability to proliferate to over 140 population doublings. Thus, the as-filed specification does not provide adequate support for the amended claims and newly added claim.

Thus, the amended claims and newly added claim include new matter.

Conclusion

No claims are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH

shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

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For all other customer support, please call the USPTO Call Center (UCC) at 800-786-9199.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anne-Marie Falk whose telephone number is (571) 272-0728. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras, can be reached on (571) 272-4517. The central official fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to (571) 272-0547.

Anne-Marie Falk, Ph.D.

/Anne-Marie Falk/
Primary Examiner, Art Unit 1632